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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/622,353

09/12/00

ARBUCKLE

J

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HM12/0621

EXAMINER

TUNG, J

ART UNIT

PAPER NUMBER

1656

DATE MAILED:

06/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.  
**09/622,353**

Applicant(s)  
**Arbuckle et al.**

Examiner  
**Joyce Tung**

Art Unit  
**1656**



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_\_
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 20) ☐ Other:

Art Unit: 1656

### **DETAILED ACTION**

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1656.

#### ***Specification***

1. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

#### ***Claim Objections***

2. The numbering of claims is not accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 16-20 have been renumbered as claims 18-21 which are used in this Office action.

#### ***Claim Rejections - 35 U.S.C. § 112***

Art Unit: 1656

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-21 are vague and indefinite because of the language "a transposable element derived sequence" and "an adapter derived sequence" in claims 1 and 15, and the language "said genomic insertion-derived sequence" and "a transgene-derived sequence" in claim 15. It is unclear what is meant by the language "derived" used in the language since by in large the language "derived" is meant by a chemical modification of a compound in the art. It is suggested to clarify the language.

- ✓ b. Claim 6 is vague and indefinite because of the language "derived from". it is unclear with the same reason as set forth in section 4(a). It is suggested to clarify the language.

c. Claims 9-10 are vague and indefinite because of the language "said preliminary <sup>Keep</sup> amplification" and "said insertion sequence". It is unclear where the language is referred from.

- ✓ d. Claim 13 is vague and indefinite because of the language "said first genomic DNA sample of step (b)" and "said second genomic DNA sample". It is unclear where the language is referred from. It is suggested to clarify the language.

Art Unit: 1656

/ e. Claims 15-21 are vague and indefinite because of the language "a DNA sample" in step (c) of claim 15. It is unclear whether or not the DNA sample is referred from genomic DNA sample of step (a). In addition, it is also unclear where the language "said inserted locations of said transgene" in step (e) of claim 15 is referred from. It is suggested to clarify the language.

1656 f. Claims 17 and 18-19 are vague and indefinite because of the language "said preliminary amplification" in claim 17.

/ g. Claim 16 is vague and indefinite because the claim 16 after claim 17 is renumbered as claim 18 which is depend from claim 16. It is suggested to make sure that the dependency of the renumbered claim 18 is correct.

***Claim Rejections - 35 U.S.C. § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

Art Unit: 1656

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 4-8, 10-13, 15-16 and 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Straus et al. (Proc. Natl. Acad. Sci. USA, 1990, Vol. 87, pg. 1889-1893) in view of Lindemann et al. (5,958,738), Walbot et al. (Mol. Gen. Genet., 1988, Vol, 211, pg. 27-34) and Briggs et al. (5,962,764).

Straus et al. disclose a method called genomic subtraction for isolating DNA that is absent in deletion mutants. The method involves reassociating the denatured wild-type and biotinylated mutant in a mixture. After reassociation, the biotinylated sequences are removed by binding to avidin coated beads. This subtraction process is then repeated several times. In each cycle, the unbound wild-type DNA from previous round is hybridized with fresh biotinylated deletion mutant DNA. The unbound DNA from the final cycle is ligated to adaptors and amplified by using one strand of the adaptor as a primer in the polymerase chain reaction (See the Abstract). This suggests that mutant DNA and wild type DNA are involved in the method (as recited in step (b) of claim 1)

Straus et al. do not disclose fragmenting one of the mutant and the wild-type genomic DNA. Straus et al. disclose that yeast strain T1753 and the derivative of the strain T1753 which is TD33.3 has deletion at the *lys2* locus. These strains contain the *Bgl* II fragment. Therefore, this suggests that the DNA sample will be digested with the restriction enzyme (See 1889, column 2, first paragraph) for fragmentation.

Art Unit: 1656

Nevertheless, Lindemann et al. disclose a method for obtaining polynucleotides comprising sequences which differ between two populations of DNA is provided (See the Abstract). The method involves using fragmentation of a polynucleotide subjected the population to the action of a restriction endonuclease (See column 13, lines 19-22) (as recited in step(c) of claim 1 and step (b) of claim 15).

Straus et al. do not disclose amplifying both wild-type DNA population and mutant DNA population with more than one primers.

Lindemann et al. disclose involving two polynucleotide populations fragmented (as recited in claims 1, 15, and 20) which are attached an oligonucleotide comprising nested primer binding sites or the complements thereof in which the primer binding sites comprising an outermost primer binding site, an innermost primer binding site and at least one more internal primer binding site between to produce marked sample and control sample (See column 10, lines 26-48). The teachings of Lindemann et al. suggest that the primer is nested as recited in step (e) of claim 1 and step (d) of claim 15 and the oligonucleotide of Lindemann et al. has the same function as the recited adapter in steps (d)-(e) of claim 1 and steps (c)-(d) of claim 15 and claim 10

None of the references of Straus et al. and Lindemann et al. discloses that the genetic sequence from an organism has disruption of genomic DNA of the organism by a transposable element flanking genetic sequence associated with a mutant phenotype and the amplified products comprising the genetic sequence flanked by a transposable element derived sequence, the

Art Unit: 1656

transposable element comprises a terminal inverted repeat sequence (TIR) which is member of Mutator family, the primer is a Mutator-TIP derived primer, the organism is plants and which is a maize plant.

Walbot et al. disclose that the Mutator stock of maize has its high mutation frequency and the characterization of an unstable allele for a Mutator identified by a new transposable element family: the *adh1*-S3034 allele contained an insertion of about 1.4 kb, termed *Mu1* which was shown to be 1,367 bp long with 213 and 215 bp terminal inverted repeats and 9bp host sequence duplication at the site of its insertion. By DNA hybridization to genomic DNA from Mutator plants, *Mu1* defines at least two families of transposable elements whose members share homology to the repetitive termini and middle portion of this element; these related sequences are called *Mu1*-like elements, and are typically found in 10-50 copies in Mutator stocks (See pg. 211, column 1, first paragraph). Complete digestion of *HinfI* restriction sites in the terminal inverted repeat sequences is characteristic of *Mu* elements in active lines, while masking of these *HinfI* is characteristic of two types of inactive *Mu* elements (See pg. 27, column 2, second paragraph). The classification for *Mu* copy in three types: active, weakly active and inactive is based on two criteria: extent of somatic mutability at a reporter allele and modification of the *HinfI* sites in the terminal inverted repeats of the *Mu* elements (See pg. 28, column 1, first paragraph). Slot blot DNA hybridization was used and the *Mu* probe was pA/B5 containing a 650 bp internal fragment of *Mu1* and a 2.3 kb *HindIII* fragment of pADH221 was used as the *adh1* gene probe (See pg. 28, column 2, first paragraph).



Art Unit: 1656

Walbot et al. do not disclose using polymerase chain reaction in which the primer is a Mutator-TIR primer derived from the TIR sequence as claimed in claims 6, 11 and 20.

Briggs et al. disclose a method for determining the function of a gene involving using the highly active Mutator family of transposable elements as a means of minimizing the number of F1 plants required to ensure a desired insertion event (See column 4, lines 22-26). Most transposable elements carry terminal inverted repeat (TIR) sequences located at each terminus of the transposable element but inverted with respect to each other (See column 4, lines 61-65). Genomic DNA isolated from the F1 plants is used as target within a gene of known sequence is detected by using one primer complementary to the gene of interest, and in a preferred embodiment, one primer complementary to the terminal inverted repeat sequence of the transposable element is used for the detection (See column 6, lines 7-13). This suggests that primer is a Mutator-TIR primer derived from the TIR sequence (as recited in claims 6).

The instant invention do not have the steps disclosed in any of the references that the denatured wild-type DNA of Straus et al. (or amplified control fragment population of Lindemann et al.) and the mutant DNA of Straus et al. (or amplified sample fragment population of Lindemann et al.) are annealed, and then subjected to amplification reaction (See pg. 1891, column 1, fig. 1 of Straus et al. and column 10, lines 49-63 of Lindemann et al.). However, the claim language "comprising" is used and this suggests that any steps will be added to perform the method. In addition, Lindemann et al. disclose that the method is for obtaining a polynucleotide fragment comprising a unique sequence in a sample population, but it is not in a control

Art Unit: 1656

population (See column 10, lines 26-48). These steps do not include the step of the annealing (See column 10, lines 26-48) (as recited in claims 1 and 15).

None of the references discloses the limitation of claim 13. Since the claim language of claim 13 is vague and indefinite as set forth in section 4(d), the language is interpreted as that the first DNA sample is wild type-DNA and the second DNA sample is mutant DNA. Lindemann et al. disclose that the DNA sample is from a population (See column 10, lines 26-30). This suggests that at least more than one organism is involved in the method.

The teachings of Straus et al., Lindemann et al., Walbot et al. and Briggs et al. suggest the limitations of claims 1, 4-8, 10-13, 15-16 and 18-21. Claims 1, 4-8, 10-13, 15-16 and 18-21 are drawn to a method of identifying and isolating a genetic sequence from an organism in which the genomic DNA is disrupted by a transposable element flanking the genetic sequence associated with a mutant phenotype. The method comprises segregating a plurality of organism by the presence or absence of the mutant phenotype comprising at least one copy of the transposable element, obtaining a mutant genomic DNA and a wild-type genomic DNA sample. fragmenting the DNA sample of mutant and wild type DNA, attaching an adaptor to the mutant DNA and the wild type DNA, amplifying the mutant and wild-type adapter-modified DNA fragments and isolating the amplified products. The amplified products comprise the genetic sequence flanked by a transposable element derived sequence and adapter derived sequence. The amplification employs at least two primers in which one of the primer hybridizes to the adapter and another one hybridizes to the transposable elements. The transposable elements comprise TIR sequences, a

Art Unit: 1656

member of the *Mutator* family. The primer is a Mutator-TIR primer derived from the TIR sequence. The organism is a maize plant.

One of ordinary skill in the art at the time of the instant invention would have been motivated to combine the teachings of Straus et al., Lindemann et al., Walbot et al. and Briggs et al. to make instant invention with a reasonable expectation of success because the method of Straus et al. involves genomic subtraction which can be used to efficiently isolate the DNA that is absent in a yeast deletion mutant (See pg. 1889, column 1, third paragraph), the method of Lindemann et al. overcomes the disadvantage in the method of use fewer PCR cycles, nuclease digestion before amplification and a single adapter designed for use with multiple primers (See column 5, lines 52-55). Walbot et al. disclose the probe to analyze *Mu* copy number in the *Mu* elements (See pg. 28, column 1, first paragraph) contains internal fragment of *Mu*1 and *Hind* III fragment is used as a probe and is in the terminal inverted repeat sequence of characteristic of *Mu* elements in active lines (See pg. 27, column 2, second paragraph). The method of Briggs et al. is the development of a rapid, inexpensive method for determining the function of a gene of known sequence (See column 3, lines 15-19) involving a primer complementary to the TIP sequence of the transposable element (See column 6, lines 7-13). Thus it would have been prima facie obvious for one of ordinary skill in the art to combine the teachings of Straus et al., Lindemann et al., Walbot et al. and Briggs et al. to make instant invention with a reasonable expectation of success as claimed.

Art Unit: 1656

7. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Straus et al. (Proc. Natl. Acad. Sci. USA, 1990, Vol. 87, pg. 1889-1893) in view of Lindemann et al. (5,958,738), Walbot et al. (Mol. Gen. Genet., 1988, Vol. 211, pg. 27-34) and Briggs et al. (5,962,764) as applied to claims 1, 4-8, 10-13, 15-16 and 18-21 above, and further in view of Grunder et al. (J. of Hypertension, 1997, Vol. 15(2), pg. 173-179).

The teachings of Straus et al., Lindemann et al., Walbot et al. and Briggs et al. are set forth in section 6 above and do not teach using cosegregation analysis to isolate an amplification product that cosegregates with said mutant phenotype as claimed in claim 2.

Grunder et al. disclose that cosegregation analysis was performed to test for correlations between blood pressure and different genotypes. (See pg. 173, column 1, third paragraph).

The teachings of Straus et al., Lindemann et al., Walbot et al., Briggs et al. and Grunder et al. suggest the limitations of claim 2 which further recite the limitations of claim 1. Cosegregation analysis is used to isolate an amplification product that cosegregates with said mutant phenotype.

One of ordinary skill in the art at the time of the instant invention would have been motivated to combine the teachings Straus et al., Lindemann et al., Walbot et al., and Briggs et al. and Grunder et al. to make instant invention with a reasonable expectation of success because of the motivation of applying the teachings of Straus et al., Lindemann et al., Walbot et al., Briggs et al. to make instant invention as discussed in section 6 above and in addition, the method of Grunder et al. is sensitive by stating that the correlation between blood pressure and

Art Unit: 1656

this polymorphism is excluded by applying cosegregation analysis (See pg. 173, column 2, first paragraph). It would have been prima facie obvious to carry out the method as claimed.

8. Claims 3 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Straus et al. (Proc. Natl. Acad. Sci. USA, 1990, Vol. 87, pg. 1889-1893) in view of Lindemann et al. (5,958,738), Walbot et al. (Mol. Gen. Genet., 1988, Vol. 211, pg. 27-34) and Briggs et al. (5,962,764) as applied to claims 1, 4-8, 10-13, 15-16 and 18-21 above, and further in view of Halverson et al. (5,707,809).

The teachings of Straus et al., Lindemann et al., Walbot et al. and Briggs et al. are set forth in section 6 above and do not teach using bulked segregant analysis to isolate the amplified products as claimed in claim 3 and labeled primer as claimed in claim 14.

Halverson et al. disclose a method for sex identification involving bulked segregant analysis (See column 21, lines 23-26) and that the primer used is joined to a label (See column 38, lines 23-25).

The teachings of Straus et al., Lindemann et al., Walbot et al., Briggs et al. and Halverson et al. suggest the limitations of claims 3 and 14. Claims 3 and 14 recite further limitations to claim 1 in which bulked segregant analysis is used to isolate the amplified products as claimed in claim 3 and the labeled primer is used as claimed in claim 14.

One of ordinary skill in the art at the time of the instant invention would have been motivated to combine the teachings Straus et al., Lindemann et al., Walbot et al., Briggs et al. and Halverson et al. to make instant invention with a reasonable expectation of success because of

Art Unit: 1656

the motivation of applying the teachings of Straus et al., Lindemann et al., Walbot et al., and Brigg et al. to make instant invention discussed in section 6 above and in addition the method of Halverson et al. is simple, accurate and efficient (See column 25, lines 17-20). It would have been prima facie obvious to carry out the method as claimed.

9. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached at (703) 308-1152.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1656 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

June 19, 2001

